

Claims

1. Method for detecting disease-associated autoantibodies, which are directed at G protein-coupled receptors,
characterized in that
the method comprises the following steps:
 - a) Bringing bodily fluid into contact with a denaturing agent,
 - b) Bringing the precipitated fraction into contact with a peptide, particularly one comprising biotin, which comprises a partial sequence of the first and/or second loop of the receptor, whereby a mixture is formed,
 - c) Incubating the mixture with a carrier coated with avidin or streptavidin,
 - d) Washing the materials of the carrier,
 - e) Incubating the carrier with anti-IgG antibody subclasses, whereby the anti-IgG antibody is marked, and
 - f) Carrying out an enzyme reaction or color reaction.
2. Method of claim 1,
characterized in that
the denaturing agent is ammonium sulfate and/or alcohol.
3. Method of claim 1,
characterized in that
the carrier is a magnetic particle or an ELISA plate.
4. Method of claim 1 or 2,
characterized in that
the autoantibodies are directed against a beta1-adrenergen receptor, a muscarinergen M2 receptor, an angiotensin II AT1 receptor, an alpha1-adrenergen receptor, and an endothelin IA receptor, a PAR-1, PAR-2, and/or PAR-3.

5. Method of one of claims 1 to 4,

characterized in that

the autoantibodies directed against the betal-adrenergen receptor are associated with dilatative myocardiopathy, Chagas' myocardiopathy, or myocarditis; the autoantibodies directed against the muscarinergen M2 receptor are associated with dilatative myocardiopathy and/or Chagas' cardiomyopathy; the autoantibodies directed against the angiotensin II AT1 receptor are associated with preeclampsia, humoral kidney rejection, and/or malignant hypertension; the autoantibodies directed against the alpha1-adrenergen receptor are associated with essential hypertension, refractory hypertension, pulmonary hypertension and/or psoriasis; and/or the autoantibodies directed against endothelin IA receptor, PAR-1, PAR-2 and/or PAR-3 are associated with Raynaud's syndrome.

6. Method of one of the preceding claims,

characterized in that

the peptide that comprises a sequence or partial sequence of the first and/or second loop of the receptor is used in the detection of dilatative myocardiopathy, myocarditis, essential hypertension, refractory hypertension, pulmonary hypertension, or psoriasis, and that the peptide that comprises a sequence or partial sequence of the second loop of the receptor is used for Chargas' myocardiopathy, dilatative cardiomyopathy, humoral kidney rejection, and/or Raynaud's syndrome.

7. Method of one of the preceding claims,

characterized in that

- the autoantibodies associated with dilatative cardiomyopathy are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the beta1-adrenergen receptor,
- the autoantibodies associated with Chargas' cardiomyopathy are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the beta1-adrenergen receptor,

- the autoantibodies associated with myocarditis are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the beta1-adrenergen receptor,
- the autoantibodies associated with dilatative cardiomyopathy are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the muscarinergen M2 receptor,
- the autoantibodies associated with Chargas' cardiomyopathy are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the muscarinergen M2 receptor,
- the autoantibodies associated with preeclampsia are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the angiotensin II AT1 receptor,
- the autoantibodies associated with humoral kidney rejection are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the angiotensin II AT1 receptor,
- the autoantibodies associated with malignant hypertension are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the angiotensin II AT1 receptor,
- the autoantibodies associated with essential hypertension are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the alpha1-adrenergen receptor,
- the autoantibodies associated with refractory hypertension are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the alpha1-adrenergen receptor,
- the autoantibodies associated with pulmonary hypertension are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the alpha1-adrenergen receptor,
- the autoantibodies associated with psoriasis are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the alpha1-adrenergen receptor,

- the autoantibodies associated with Raynaud's syndrome are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the endothelin IA receptor, PAR-1, PAR-2 and/or PAR-3.

8. Method of one of the preceding claims,
characterized in that
the IgG subclasses are IgG1, IgG2, IgG3 and/or IgG4 subclasses.

9. Method of one of the preceding claims,
characterized in that

- in the case of dilatative cardiomyopathy, the IgG3 and/or IgG4 subclasses are used if the peptide comprises a sequence or partial sequence of the first loop, and/or the IgG1 subclass is used if the peptide comprises a sequence or partial sequence of the second loop,
- in the case of Chagas' cardiomyopathy, the IgG1, IgG2, IgG3 and/or IgG4 subclasses are used,
- in the case of myocarditis, the IgG3 and/or IgG4 subclasses are used if the peptide comprises a sequence or partial sequence of the first loop, and/or the IgG1 subclass is used if the peptide comprises a sequence or partial sequence of the second loop,
- in the case of preeclampsia, the IgG3 subclass is used,
- in the case of humoral kidney rejection, the IgG1 and IgG3 subclasses are used,
- in the case of malignant hypertension, the IgG1 and/or IgG3 subclasses are used,
- in the case of essential hypertension, the IgG1 and/or IgG3 subclasses are used if the peptide comprises a sequence or partial sequence of the first loop, and/or the IgG2 subclass is used if the peptide comprises a sequence or partial sequence of the second loop,
- in the case of refractory hypertension, the IgG1 and/or IgG3 subclasses are used if the peptide comprises a sequence or partial sequence of the first loop, and/or the IgG2 subclass is used if the peptide comprises a sequence or partial sequence of the second loop,

- in the case of pulmonary hypertension, the IgG1, IgG2, IgG3 and/or IgG4 subclasses are used,
- in the case of psoriasis, the IgG1, IgG2, IgG3 and/or IgG4 subclasses are used, and/or
- in the case of Raynaud's syndrome, the IgG1 subclass is used.

10. Method of one of the preceding claims,
characterized in that
the autoantibodies are concentrated or purified before being identified.

11. Method of the preceding claim,
characterized in that
the method for concentrating or purifying the autoantibodies comprises the following steps:

- a) Obtaining an IgG fraction from bodily fluid,
- b) Bringing the IgG fraction that was obtained into contact with a peptide that comprises a partial sequence of a first or second loop of a G protein-coupled receptor, whereby a mixture is obtained,
- c) Incubating the mixture with a carrier that is washed and concentrated, and
- d) Eluting the autoantibodies from the concentrated carrier.

12. Method of one of the preceding claims,
characterized in that
the peptide that comprises the sequence or partial sequence of the first and/or second loop is selected from the group comprising EYGSFF, SFFCEL, ARRCYND, PKCCDF, AESDE, CYIQFF, EDGECY, VRTVEDGEICYIQFFSNAAVTFGTAI, AFHYESQ, ENTNIT, FWAFGR, GRAFCDV, ITEEAGY, ERFCGI, GRIFCD and/or ITTCHDVL.

13. Method of the preceding claim,
characterized in that
the peptide comprises amino groups, amides, acetyl groups, biotin groups, markers, spacers, linkers, GKK and/or SGKK.

14. Method of the preceding claim,
characterized in that
the linker and/or the spacer are selected from the group comprising α -amino carboxylic acids as well as their homo-oligomers and hetero-oligomers; α,ω -amino carboxylic acids as well as their branched homo-oligomers and hetero-oligomers; other amino acids as well as the linear and branched homo-oligomers and hetero-oligomers; amino-oligoalkoxy alkyl amines; maleinimido carboxylic acid derivatives; oligomers of alkyl amines; 4-alkylphenyl derivatives; 4-oligoalkoxy phenyl or 4-oligoalkoxy phenoxy derivatives; 4-oligoalkyl mercaptophenyl or 4-oligoalkyl mercaptophenoxy derivatives; 4-oligoalkyl aminophenyl or 4-oligoalkyl aminyphenoxy [sic] derivatives; (oligoalkylbenzyl) phenyl or 4-oligoalkylbenzyl phenoxy derivatives as well as 4-oligoalkoxy benzyl phenyl or 4-oligoalkoxybenzyl phenoxy derivatives; trityl derivatives; benzyloxyaryl or benzyloxyalkyl derivatives; xanthen-3-yl oxyalkyl derivatives; (4-alkyl phenyl) or ω -(4-alkyl phenoxy) alkanic acid derivatives; oligoalkyl phenoxy alkyl or oligoalkoxy phenoxy alkyl derivatives; carbamate derivatives; amines; trialkyl silyl or dialkyl alkoxy silyl derivatives; alkyl or aryl derivatives and/or combinations thereof.

15. Method of one of the preceding claims,
characterized in that
the peptide is modified by means of deletion, addition, substitution, translocation, inversion and/or insertion.

16. Peptide selected from the group comprising EYGSFF, SFFCEL, ARRCYND, PKCCDF, AESDE, CYIQFF, EDGEKY, VRTVEDGEKYIQFFSNAAVTFGTAI, AFHYESQ, ENTNIT, FWAFGR, GRAFCDV, ITEEAGY, ERFCGI, GRIFCD and/or ITTCHDVL, for use as a medicinal active substance.

17. Peptide of the preceding claim,
characterized in that
the peptide is bound by autoantibodies of patients having one of the following diseases: dilatative cardiomyopathy, Chagas' cardiomyopathy, myocarditis, preeclampsia,

humoral kidney rejection, malignant hypertension, essential hypertension, refractory hypertension, pulmonary hypertension, psoriasis and/or Raynaud's syndrome.

18. Peptide of claim 15 or 16,
characterized in that
the peptide is immobilized.
19. Peptide of the preceding claim,
characterized in that
the peptide the peptide is bound to a solid phase.
20. Recognition molecule directed against the peptide of one of claims 16 to 19.
21. Recognition molecule of the preceding claim,
characterized in that
it is an antibody, a lectin, an antisense construct, and/or a chelator.
22. Pharmaceutical composition comprising a peptide of one of claims 16 to 19 and/or a recognition molecule of claim 20 or 21.
23. Kit comprising a peptide of one of claims 16 to 19, a recognition molecule of claim 20 or 21, and/or a pharmaceutical composition of claim 22, if applicable with instructions for combining the contents of the kit and/or for making available a formulation.
24. Chromatography device comprising peptides of one of claims 16 to 19 and/or recognition molecules of claim 20 or 21.
25. Device of the preceding claim,
characterized in that
the peptides are bound to the solid phase.

26. Use of the peptides of one of claims 16 to 19 and/or recognition molecules of claim 20 or 21 and/or a pharmaceutical composition of claim 22 and/or a kit of claim 23 and/or a device of claim 24 to 25 for the prophylaxis, diagnosis, therapy, monitoring the progression as well as follow-up treatment of autoimmune diseases selected from the group comprising dilatative cardiomyopathy, Chagas' cardiomyopathy, myocarditis, preeclampsia, humoral kidney rejection, malignant hypertension, essential hypertension, refractory hypertension, pulmonary hypertension, psoriasis and/or Raynaud's syndrome.
27. Use of the peptides of one of claims 16 to 19 and/or recognition molecules of claim 20 or 21 and/or a pharmaceutical composition of claim 22 and/or a kit of claim 23 and/or a device of claim 24 to 25 for the production of a medication for the treatment of autoimmune diseases selected from the group comprising dilatative cardiomyopathy, Chagas' cardiomyopathy, myocarditis, preeclampsia, humoral kidney rejection, malignant hypertension, essential hypertension, refractory hypertension, pulmonary hypertension, psoriasis and/or Raynaud's syndrome.
28. Use of the peptides of one of claims 16 to 19 and/or recognition molecules of claim 20 or 21 and/or a pharmaceutical composition of claim 22 and/or a kit of claim 23 and/or a device of claim 24 to 25 for screening medications.
29. Use of the peptides of one of claims 16 to 19,
characterized in that
autoantibodies directed against betal-adrenergen receptor, muscarinergen M2 receptor, angiotensin II AT1 receptor, alphal-adrenergen receptor, endothelin IA receptor, PAR-1, PAR-2, and/or PAR-3 are detected, bound, complexed and/or neutralized.
30. Method for treating an autoimmune disease,
selected from the group comprising dilatative cardiomyopathy, Chagas' cardiomyopathy, myocarditis, preeclampsia, humoral kidney rejection, malignant hypertension, essential hypertension, refractory hypertension, pulmonary hypertension, psoriasis, Raynaud's syndrome, by means of binding and/or removing antibodies by means of peptides of one of claims 16 to 19, bound to a solid phase.

31. Method of the preceding claim,
characterized in that

the autoantibodies are directed against betal-adrenergic receptors in the case of dilatative cardiomyopathy, against betal-adrenergic receptors in the case of Chagas' cardiomyopathy, against betal-adrenergic receptors in the case of myocarditis, against muscarinic M2 receptors in the case of dilatative cardiomyopathy, against muscarinic M2 receptors in the case of Chagas' cardiomyopathy, against angiotensin II AT1 receptors in the case of preeclampsia, against angiotensin II AT1 receptors in the case of humoral kidney rejection, against angiotensin II AT1 receptors in the case of malignant hypertension, against alpha1-adrenergic receptors in the case of essential hypertension, against alpha1-adrenergic receptors in the case of refractory hypertension, against alpha1-adrenergic receptors in the case of pulmonary hypertension, against alpha1-adrenergic receptors in the case of psoriasis, and that the autoantibodies are directed against endothelin IA, PAR-1 PAR-2 and/or PAR-3 in the case of Raynaud's syndrome.